HIGHLIGHT

Confining Nanopore Bipolar Electrochemical Processes to Give Pattern in Space and Time

Frank Marken*[a]

The recent implementation of nanopore-based detection for single molecules such as DNA, proteins, and other biopolymers, propelled nanopore electrochemistry to a highly prominent status.[1,2,3] The nanopore-based detection method is based on a highly confined electrochemical space for real time analysis of single-molecule characteristics, which include structure, interactions, conformational changes, and distinguishing functional groups.[4,5,6] However, in nanopore processes usually only the net ionic flux is monitored. It is still challenging to detect both ion flux and accompanying "bipolar" redox reactions in conjunction. Related and very interesting attempts to introduce bipolar detection processes in nanopores have been reported for example by Albrecht and coworkers[7,8] and by Bohn and coworkers.[9] The electrochemical detection with metal-based nanopores,[10] with graphene-based nanopores,[11] and with bipotentiostatically controlled probe electrodes at nanopores has been proposed.[12,13]

After making many pioneering contributions to nanopore-based single molecule electroanalysis,[4,5,6,14,15] Professor Yi-Tao Long and his research team at East China University of Science and Technology (ECUST) now proposed the concept of "confining electrochemistry" into a nanopore space to add a new experimental approach in the challenge of electrochemical detection at single molecule level. They developed a "wireless" metal-coated nanopore electrode, which could not only combine ion flux with redox conversion of analytes at the opening of nanopores, but also convert the Faradaic current response into a more easily distinguishable bubble-induced transient ionic current response pattern (Figure 1).[16,17]

As a proof-of-principle model system, a silver-coated nanopore pipette configured as a "wireless" nanoelectrode was utilized to detect the formation of "co-generated" H_2 and Ag^+. In bipolar electrochemistry, when the potential difference of the conductive silver layer (see Figure 1) from one terminal to the other reaches a minimum potential difference for the two electrochemical reactions to occur, the coupled redox reactions generating H_2 and Ag^+ can take place. Spike-shaped current signals could be observed. The numerical simulation analysis of experiments revealed that the spike-shaped signals are associated with oscillations in the ionic current due to the generation of H_2 at the opening of the nanopore. Inspired by this phenomenon, the addition of competitive electroactive analytes were investigated. For example, after the addition of trace amounts of Hg^{2+}, the decrease of the spike signal frequency was observed. This relates back to the reduction of Hg^{2+}, which occurs prior to the reduction of H^+. The H_2 bubble dynamics are therefore linked to the presence of traces of Hg^{2+}.

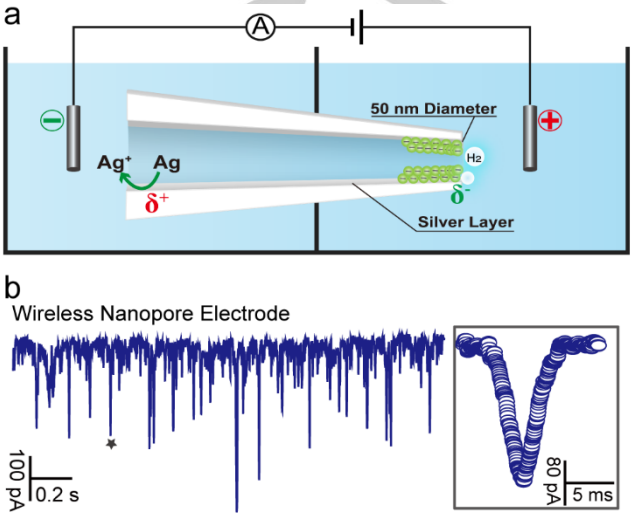

Figure 1. (a) Illustration of a silver-coated nanopore electrode. The 50 nm-diameter quartz nanopore is pulled by the P-2000 laser puller. The silver layer on the inner wall of the nanopore is fabricated by the magnetron sputtering technology[17] or by electron beam evaporation[16]. The silver layer is polarized under the applied potential provided by a pair of Ag/AgCl electrodes. Generally, the electrode on the tail/open side of the nanopore is defined as a working electrode while the other one is defined as the virtual ground. When the potential difference of two termini of the silver layer reaches the potential difference of the oxidation of silver and the reduction of H^+, the two reactions take place simultaneously. (b) An example for a raw ionic current trace for the silver-coated nanopore electrode at -800 mV. The star symbol denotes a typical spike-shaped current signal shown expanded in the insert.

Owing to the asymmetric morphology of the nanopore, there is an enhanced electric field in the confined space with an electrochemical process driven at both ends. A bipolar electrochemical reaction takes place connecting the two termini of the metal layer. Although the electrochemical reaction occurs complementing the ion flux, the electron transfer process is hard to monitor directly without resort to time domain methods. However, bubble-induced ionic current oscillation provide an advantageous nanopore detection mechanism due to nano-bubbles disturbing the confined space. Extremely low levels of analytes (e.g. Hg^{2+}) potentially down to single ion levels affect the nano-bubble formation in this confined space and therefore modulate the electrochemical response pattern.

The nanopore electrode diameter can be readily varied by changing the nanopipette pulling parameters to give sizes of the nanopore tip from 50 nm to 200 nm. Compared to the fabrication process for traditional nano-electrodes, the flexible size range of this bipolar nanoelectrode provides an opportunity to adjust conditions to potentially analyse a diverse range of electroactive

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molecules. The controllable size and ease of fabrication of this bipolar nanoelectrode may also help improving repeatability in nano-electroanalysis.

In addition to the temporal pattern induced by nano-bubble formation in the confined nanopore space, also spatial pattern in the form of nano- and micro-electrogenerated structures can be observed. Recently, the bipolar nanopore electrode could be utilized for micro-scale fabrication of micro-rings of self-assembled nanoparticles. Yi-tao Long and co-workers developed a bipolar nanopore-based method for making homogeneous solutions of micro-cyclic structures of the gold nanoparticles (Figure 2). [17] This electrochemically driven self-assembly method involved a simple and classic organic coupling reaction based on Ag^+ and terminal alkynyls as an elementary reaction during the organization process.

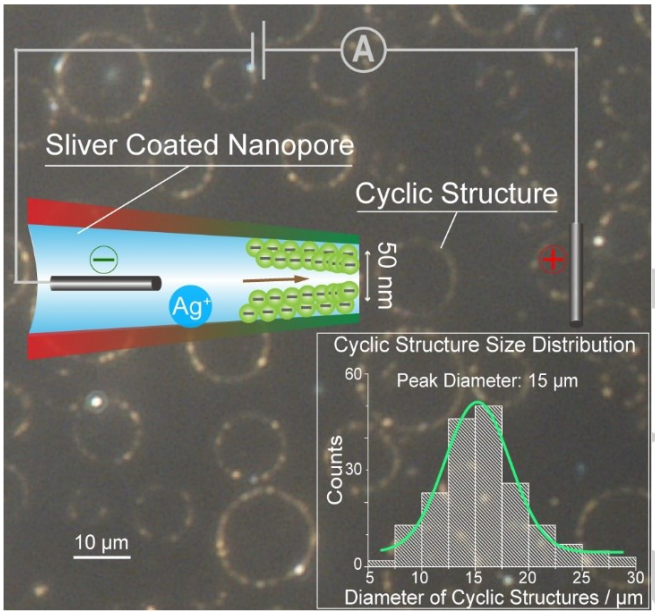

Figure 2. Illustration of a silver-coated nanocone with potential-induced nanoparticle self-assembly. The 50 nm diameter quartz nanopore is pulled with a P-2000 laser puller. The silver layer on the inner wall of the nanopore is fabricated by the magnetron sputtering technology. The 14 nm-diameter functionalized gold nanoparticles (with terminal alkyne) are added into the bulk solution. Due to diffusion of electro-generated silver ions from the nanopore, the nanoparticles could assemble to micro-cyclic structures with the diameter of typically 15 μm, which is in agreement with the diffusion profile of the silver ions at the nano-pipette orifice.

It was postulated that the electro-generated Ag^+ from the bipolar nanopore reaction could diffuse-migrate from the pipette into the solution (possibly associated with electroosmotic flow and affected by nano-bubble dynamics). With the help of a classic organic reaction between terminal alkynyl compound and silver ions, the terminal alkyne functionalized gold nanoparticles could assemble into uniform micro-cyclic structures in a highly ordered/localized assembly process. The size distribution of the cyclic structures was suggested to be associated with the diffusion profile of silver ions at the nano-pipette tip.

This method introduced a simple but very direct approach to the fabrication of micro-structures with micro-ring morphology. In recent years, large-scale assembly of nanoparticles has attracted increasing attention owing to the widespread practical applications such as plasmonic sensing, catalysis, and drug delivery. Nowadays, the existing self-assembly methods face many restrictions including the fabrication of templates and the homogeneity of the self-assembly structure. The new bipolar nanopore electrochemistry strategy is template-free and nanofluidic in nature. Attempts to generate micro-rings by simply mixing the gold nanoparticle precursor and Ag^+ failed. With an electrochemical driving force the localized self-assembly process generated micro-rings products with high homogeneity.

Both, the analytical applications of the temporal pattern in ionic current responses and the micro-structuring based on spatial pattern provide intriguing examples of how highly localized/confined redox processes can be exploited. In future, both could be applied for a wider range of systems.

Beyond the nano- and/or micro-fabrication applications, this new electrochemical technique could be utilized in bio-analysis and for single cell detection. Specific cellular reactions could be directly and high-sensitively read out by precisely inserting nanopores into individual cells similar to methods employing nanoelectrodes.[18] The pore-forming material, quartz, remains extraordinary versatile with chemically inert and perfect optical characteristics. The concept of confined space electrochemistry and the wireless nanopore electrode could be further expanded to optical even electro-optical synergistic confined space for nano-spectroelectrochemistry. We expect more advances and contributions to analytical applications in nanoscience and in analytical science.

Keywords: wireless nanopore electrode, confined electrochemistry, single molecule detection

References

[1] D. Deamer, M. Akeson, D. Branton, *Nat. Biotechnol.* **2016**, *34*, 518-524.
[2] I. Makra, R.E. Gyurcsanyi, *Electrochem. Commun.* **2014**, *43*, 55-59.
[3] N. N. Liu, Z. K. Yang, X. W. Ou, B. M. Wei, J. T. Zhang, Y. M. Jia, F. Xia, *Microchim. Acta* **2016**, *183*, 955-963.
[4] Y. Long, M. Zhang, *Sci. China Ser. B-Chem.* **2009**, 52: 731-733.
[5] Y. L. Ying, J. Zhang, R. Gao, Y. T. Long, *Angew. Chem. Int. Ed.* **2013**, *52*, 13154-13161.
[6] C. Cao, Y. L. Ying, Z. L. Hu, D. F. Liao, H. Tian, Y. T. Long, *Nat. Nanotechnol.* **2016**, *11*, 713-718.
[7] T. Albrecht, *ACS Nano* **2011**, *5*, 6714-6725.
[8] A. Rutkowska, K. Freedman, J. Skalkowska, M. J. Kim, J. D. Edel, T. Albrecht, *Anal. Chem.* **2015**, *87*, 2337-2344.
[9] C. X. Ma, L. P. Zaino, P. W. Bohn, *Chem. Sci.* **2015**, *6*, 3173-3179.
[10] M. Ayub, A. Ivanov, E. Instuli, M. Cecchini, G. Chansin, C. McGilvery, J. Hong, G. Baldwin, D. McComb, J.B. Edel, T. Albrecht, Electrochim. Acta **2010**, *55*, 8237-8243.
[11] G.F. Schneider, S.W. Kowalczyk, V.E. Calado, G. Pandraud, H.W. Zandbergen, L.M.K. Vandersypen C. Dekker, *Nano Lett.* **2010**, *10*, 3163–3167.
[12] M. Ayub, A. Ivanov, J. Hong, P. Kuhn, E. Instuli, J.B Edel, T. Albrecht, *J. Phys. Condens. Matter* **2010**, *22*, 454128.
[13] A. Rutkowska, J.B. Edel, T. Albrecht, *ACS Nano* **2013**, *7*, 547-555.

[14] Y. L. Ying, J. J. Zhang, F. N. Meng, C. Cao, X. Y. Yao, I. Willner, H. Tian, Y. T. Long, *Sci. Rep.* **2013**, 3, 1622.

[15] H. Y. Wang, Z. Gu, C. Cao, J. Wang, Y. T. Long, *Anal. Chem.* **2013**, 85, 8254-8261.

[16] R. Gao, Y.-L. Ying, Y.-X. Hu, Y.-J. Li, Y.-T. Long, *Anal. Chem.* **2017**, revised.

[17] R. Gao, Y. Lin, Y.-L. Ying, X. Y. Liu, X. Shi, Y. X. Hu, H. Tian, Y.-T. Long, *Small* **2017**, DOI: 10.1002/smll.201700234.

[18] Y. L. Ying, Z. F. Ding, D.P. Zhan, Y. T. Long, *Chem. Sci.* **2017**, *8*, 3338-3348.

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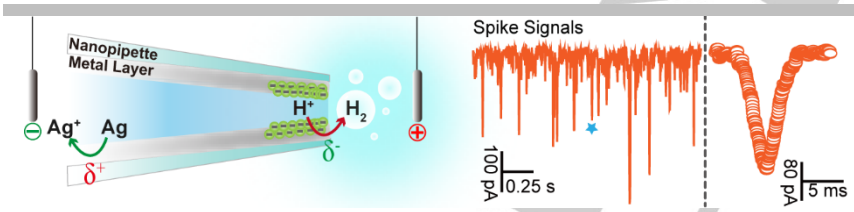

"Wireless" metal-coated nanopore electrode processes have been developed by Yi-tao Long and coworkers confining bipolar electrochemical processes into a nanopore. The reported concept of this method may lead to intriguing new analytical and micro-structuring application based on temporal pattern in ionic current responses and based on spatial pattern leading to micro-ring nano-assembly.

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